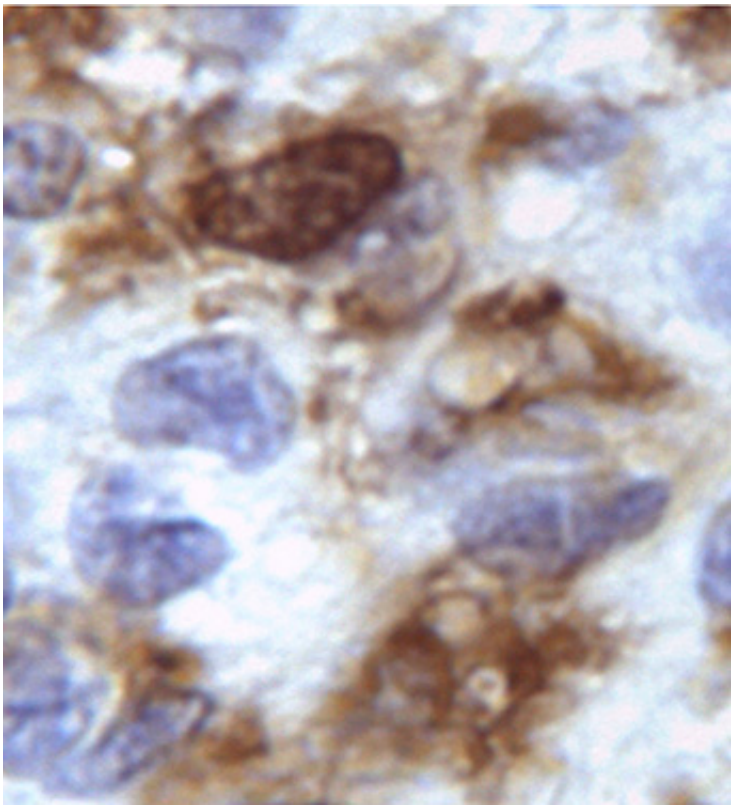
# New clue to aggressive brain tumors

October 21 2013, by Michael C. Purdy



When support cells known as monocytes, pictured in brown, make the protein F11R inside brain tumors, the cancer is more aggressive and length of survival decreases. Blocking F11R and other tumor support factors may help patients live longer, the research suggests. Credit: Winnie Pong, PhD

(Medical Xpress)—Scientists at Washington University School of Medicine in St. Louis have identified a biological marker that may help predict survival in people with deadly brain tumors. The researchers

showed that when the marker is present at higher levels, brain cancers known as glioblastomas are more aggressive.

The cancer cells do not make the marker, a protein called F11R. Instead, it is made by noncancerous cells, called monocytes, found within the tumor. Monocytes normally support and protect healthy brain cells, but they also can provide critical support to tumors.

"Monocytes are very dynamic cells, and they can adapt to changing circumstances including the development of a tumor," said senior author David H. Gutmann, MD, PhD, the Donald O. Schnuck Family Professor of Neurology. "We need to better characterize the specific contributions of these cells to brain tumors, as well as to identify treatments that block their ability to help these cancers form and grow."

The study recently is available online in *PLOS ONE.*

Glioblastomas are rare but are among the most dangerous tumors. Even with radiation and chemotherapy, the median survival rate is little more than a year.

Hoping to provide another avenue of attack for these cancers, Gutmann and his collaborators have been studying how non-cancerous cells contribute to brain cancer formation and growth.

In earlier studies, Gutmann has shown that monocytes are critical for the formation and continued growth of low-grade brain tumors in mice that resemble those arising in children with neurofibromatosis type 1 (NF1).

Winnie W. Pong, PhD, a staff scientist in Gutmann's laboratory, wanted to determine whether monocytes in the glioblastomas originate in the brain early in embryonic development or migrate into the brain from the bone marrow. Differences in where cells originate may affect their

ability to support cancer development and growth.

To address this question, Gutmann turned to Elaine Mardis, PhD, co-director of The Genome Institute at Washington University, for help. Mardis has been a leader in developing techniques for sequencing RNA, the material cells use to copy protein-building instructions from DNA. The number of RNA copies of a gene present in a cell reflects how often the cell is using the gene to make its protein.

"We asked Elaine to apply new RNA sequencing techniques to very small samples of monocytes from normal mice and from mouse glioblastomas," Gutmann said. "She and her colleagues at The Genome Institute accomplished a small tour de force to perform the analysis."

F11R emerged as one of the best indicators of whether monocytes came from the brain or from bone marrow. F11R normally is made by monocytes that originate in the brain and not by those that come from bone marrow.

However, the scientists also learned that this distinction vanishes in glioblastomas, where both types of monocytes make F11R. Gutmann reasoned that the tumor may prompt this change, suggesting that the protein could be important to cancer cells.

"When we checked for connections between F11R levels and the aggressiveness of brain tumors, we found more F11R-expressing monocytes in malignant tumors relative to their more benign counterparts," he said. "Moreover, even among the most malignant tumors we could use F11R to predict differences in patient survival rates."

To find new treatments for these deadly cancers, Gutmann and his colleagues are working to identify factors made by monocytes that help

the tumors grow.

"The idea that we may be able to starve brain cancer cells of critical growth factors produced by noncancerous support cells may one day lead to the development of additional strategies to combine with conventional chemotherapy or radiation to combat brain tumors in children and adults," he said.

**More information:** Pong, W. et al. F11R Is a Novel Monocyte Prognostic Biomarker for Malignant Glioma, *PLOS ONE*, published online Oct. 15, 2013.

Provided by Washington University School of Medicine in St. Louis